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## CONTENTS

*Editorial*:

The First Authentic Periodical of Medical History, F. H. Garrison ..... 421

The Treatment of Neurosyphilis, Harry C. Solomon..... 428

Cardiovascular Syphilis, Edwin P. Maynard, Jr..... 442

The Pathology of Syphilis, Harrison S. Martland..... 451

General Discussion, Harlow Brooks..... 472

Recent Accessions to the Library ..... 475

Deaths of Fellows of the Academy ..... 478

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# EDITORIAL

## THE FIRST AUTHENTIC PERIODICAL OF MEDICAL HISTORY

In the 18th Century, there was a remarkable and significant extension of interest in the history of medicine, which had formerly cropped out only in spots and at long intervals of time. Such manifestations as Hippocrates on ancient medicine, Menon's *Iatrika,* the *Proaemium* of Celsus, the biographical sketches of Useibia and the subsequent contributions of Guy de Chauliac, Symphorien Champier, or Conring can scarcely be regarded as influential, and for a full quarter-century thereafter, little was done to improve upon the lengthy and credulous narrative of Leclerc. A wholly uncritical approach, portentous ignorance of or indifference to the basic sources of fact, an overweening assumption of omniscience and, in consequence, a facile tendency to improvisation are outstanding traits of Leclerc and of most of his immediate followers. Foreknowledge absolute of the status of medicine before and after the Flood is taken for granted and even the worries of Noah about the provisioning of the paired animals in his Ark and the disposal of their excreta is considered in one instance. The medicine of the Chaldeans, Egyptians and Assyro-Babylonians is derived respectively from Shem, Ham and Japhet. Noah and Moses are featured as founders of chemistry. The myths of classical antiquity are accepted as literally true, and chronology is dislocated to suit the whims of the improvisator. Dates for the most insignificant happenings are assigned with a facile assurance which would be ludicrous were it not palpably childlike. Burggrav in his *Libitina* (1701), Crause (1709), Al-

bert (1711), Rangius (1716) and others debate with unblushing confidence on "the fates of medicine" (*De fatis medicinae*). Some improvement in method but certainly no advancement in knowledge has been demonstrated in the work of Barkhausen (1716, 1723), who dealt with the history of medical theories and attempted to lead back to basic sources, of Goelicke (1713-23), who was critical to the point of being ill-natured, and of Schulze (1728), who advances sound views of things, but fixes the death of Adam at 9 a.m. in 3054 B.C., assigns 2329 as the date of the Flood and 1247 for the beginning of the Aesculapian Cult.[1] In all these matters, the *mens medica* of the period was uncritical and childlike. The so-called pragmatical tendency of the later 18th Century historians, the tendency to regard practical results as the main criterion of advancement in medicine, began in England with Freind (1725-6), got its stride on the continent in Haller and culminated in the 5-volume treatise of Sprengel (1792-1803), which remained the most considerable and reliable record of our subject before the time of Haeser. Pragmatism came into being through the fact that the initial directives of 18th Century thought were no longer metaphysical but mathematical. Descartes, Spinoza, Leibnitz, and Pascal gave place to Newton, Petty, Halley, Fahrenheit, De Moivre, D'Alembert, Lagrange and La Place. Descartes (analytical geometry), Leibnitz (integral calculus) and Pascal (descriptive geometry, probabilities) were at once mathematicians and philosophers. Even in the transition period, the newer tendency had already been established by the publication of Newton's differential calculus (*Methodus fluxionum,* 1671), his *Principia* (1687), his treatise on Optics (1704), and by Locke's *Essay on the Human Understanding,* which derives knowledge from experience and established the primacy of common sense. The period of "enlightenment," which preceded the French Revolution,

[1]See the careful analyses of these obsolete Latin text-books in Edith Heischkel's Die Medizinhistoriographie im XVIII. Jahrhundert (Leiden, 1931), for which we are grateful, as no one in his senses would ever dream of attempting to read or study them.

was characterized by an universal appeal to common sense, set off by a spontaneous and unswerving belief in the progressive perfectibility of the human species. This aim was to be forwarded by steady-going utilitarianism, a glorification of rationalism, rapid circulation of new discoveries and the novel device of an appeal to the public opinion thus enlightened. In other words, the appeal was virtually to an enlightened despotism, centering usually in the ruler and bulwarked by the cultivated classes. Fontenelle and others deliberately sought to popularize science among people of fashion, very much as Huxley and Tyndall attempted the same thing later with the working classes. All this tended to heighten the self-esteem of the recipients, and thus engendered the new view of history as a stepwise progression to the summit of human perfection already attained. Thus the subject came to be developed in a rigorous, systematic way, as in the mathematics or botany. Pope's "Order is Heaven's first law" points to the *Theos geometer* of the 18th Century deists. Even Apollo, in the words of Frederick the Great, had become "Newtonized."[2] Sprengel's criterion of pragmatism was "that it makes us wiser" (*wenn sie uns klug macht*). Its object was to teach. Its means to this end centered in the formal text-book. The metaphysical view of things persisted in Germany, where the mysticism latent in Kant, Goethe (*Faust*) and Beethoven determined in advance the intellectual tendencies of German romanticism. But even during the Romantic period (1801-30), the German medical historians (including Haeser) continued in the 18th Century tradition. Their ground-plan or frame-work was that of the 18th Century systematists; their aim that of pragmatism, to *teach* and disseminate sound views of the subject *urbi et orbe;* and in this they were wise.

In keeping with the program of disseminating knowledge among the intelligentsia of the time, the 18th Century witnessed the first great upthrust of medical societies

[2] Referring to poems of Voltaire and Haller about Newton and to Mme. du Châtelet's translation of the *Principia.*

and medical periodicals, both which originated in the 17th Century. In the 17th Century, the Royal Society (London) and the Académie des sciences (Paris) became more influential and informing than Oxford or Cambridge or even the Paris Medical Faculty. The Royal Prussian Academy of Sciences (Berlin) was founded in the year 1700. At Göttingen, Haller deliberately utilized the medical society, the medical periodical and the medical library (medical bibliography) as ways and means of getting the results he was after (the essential aim of pragmatism). His exploitation of bibliography, or "taking an account of stock" of past and present achievement (*sich Rechenschaft geben*), culminated in such great enterprises as the Index Catalogue, the Royal Society Catalogue of Scientific Papers, and the Berlin Catalogue of Incunabula. Haller got the material for his four bibliographies[3] out of his own library, and, for the first time, indexed the articles in medical periodicals, utilizing, as copyists, his lady relatives and their friends, who did the work for pin-money. The medical periodicals of the 18th Century number well upwards of 100 items, and already cover such specialties as physiology, surgery, gynæcology, obstetrics, pediatrics, medical jurisprudence, public hygiene, military medicine, pharmacy, mesmerism and somnambulism, and even smallpox. Two, at least, are devoted to medical history, namely the *Archiv für Geschichte der Arzneykunde* (1790), known as Wittwer's *Archiv*, and Sprengel's *Beyträge zur Geschichte der Medicin* (Halle, 1794-6). A third, bearing the specious title *Giornale per servire alla storia ragionata delta medicina di questo secolo* (Venice, 1783-95), is, in reality, a collection of abstracts of contemporary periodical literature, many of them unsigned, with an occasional original article on theoretic medicine (Castiglioni). The same thing is true of the Parisian *Recueils periodiques* (1754-7, 1796-1802, 1799), and other 18th Century repositories or year-books of abstracted medical literature of foreign and

[3] Bibliotheca botanica, Zürich, 1771-2. Bibliotheca anatomica, 1774-77; Bibliotheca chirurgica, Berne, 1774-7. Bibliotheca medicinae practicae, Basel, 1776-8.

domestic provenance. Wittwer's *Archiv* has escaped the attention of Diepgen, Seemen, Edith Heischkel and other recent investigators of the status of medical history in the 18th Century, probably because it is a thin unpretentious octavo of 222 pages, in dingy pasteboard binding, the kind of item likely to be overlooked or shoved to the rear on library shelves, like an attenuated individual lost in a crowd. By reason of the prolonged ill health of its editor, it never got beyond the first number of volume I, which, however, was, in all probability, issued as a bound volume, complete in itself. Philipp Ludwig Wittwer, its editor, born at Nuremburg on May 19, 1752, was the son of Johann Conrad Wittwer (1725-75), an esteemed practitioner and obstetrician of Nuremberg, who published only a graduating dissertation on vomiting (1742). After some training under his father, the younger Wittwer studied medicine at the Universities of Altdorf and Strassburg, graduating from the latter institution in 1774, with a dissertation proposing an adaptation of current dispensatories or pharmacopœias to the actual needs of the time in which they were published. After a year of study in Paris, he settled down to practice in his native city, where he became a member of the local College of Physicians. During this Nuremberg period, Wittwer published a well known anthology of Strassburg medical dissertations in four volumes (1777-81). In 1873, he was called to the vacant chair of medicine at Altdorf, but, a year later, was forced to relinquish this position and return to Nuremberg on account of a nervous breakdown. The rest of Wittwer's short life was spent in prolonged travelling in search of health. He died at the age of forty on December 24, 1792. He was evidently highly esteemed in his native city, for an account of a memorial erected in his honor by the *Blumenorden* of Nuremberg, of which he was a member, was published a year after his death (1795). The catalogue of his fine library, published at Nuremberg in three volumes (1794), covers 1222 pages. The appearance of Wittwer's *Archiv* two years before his death, raises the question: did he perhaps lecture on history of medicine

during his incumbency of the Strassburg Chair? It seems possible, if not entirely probable, in the light of the investigation of Seemen,[4] which goes to show that the subject was taught at all the German universities, during the latter half of the 18th Century, while there was an actual chair of the subject in the Paris Medical Faculty, held in succession by Goulin (1795-99) and Cabanis (1799-1808). Be that as it may, Wittwer's *Archiv* is a charming little item, which ought to attract the attention of collectors. Headed by a remarkably good mezzotint of Maximilian Stoll (1742-87), and an elaborate dedication to Moehsen (one of the earliest and ablest cataloguers of medical engravings and medals), it bears, on the reverse of the title page, the following motto of Cicero: *Nescire, quid antea, quam natus sis, acciderit, id est semper esse puerum* (To be ignorant of what happened before you were born is to remain an eternal boy). Wittwer's preface is along the broadest lines. He begins with a long series of questions: What is medical history, its scope, subdivisions, sources and aims? How much or how little has been done in this field to date and why? How can it be made more pragmatical, attractive and utilizable? What are the consequences of neglecting it? How can the fragmentary findings available be fused and approximated to the idea of an universal history of medicine? All this he answers by a lengthy citation from Hensler, who notices how little has been accomplished since Freind or the introductory bibliographies of Haller, and points out that the subject must be studied by major epochs and in connection with the history of philosophy. In keeping with the cult of pragmatism, Hensler defines history as the "Light of Truth and the Teacher of Life." Wittwer then resumes, stressing his long predilection for the subject, his desire to found such a periodical as far back as 1787 and the interruption of all his plans by repeated attacks of hypochondria. He proposes that his *Archiv* shall have the widest scope, covering 1. The

[4]Hans von Seemen: Zur Kenntnis der Medizinhistorie in der deutschen Romantik. [*Beitr. z. Gesch. d. Med.* hrsg. vom Inst. f. Gesch. d. Med., Leipzig.] Zürich, Leipzig, Berlin, 1926.

general history of medicine in all its ramifications, from primitive aspects up to epidemiology, in particular the effect of climate, form of government, religion, immigration, wars and conquests, degree and extent of culture upon the status of medicine in all times and places. 2. Biographies of great medical leaders and of notorious charlatans. 3. Bibliography, i.e., descriptions of rare or important medical books and MSS., additions to Haller, etc. 4. Extracts from travels of physicians or others, who have reported upon the status of medicine among primitive peoples; unprinted letters of deceased physicians of importance; accounts of paintings, etchings, monuments and other artistic productions relating to medicine; portraits of physicians; medical medals and coins; anecdotes, queries and themata. He requests that any such material available be sent to him in care of his publishers. Each volume of the *Archiv* will consist of two numbers, prefaced by a portrait of some famous physician. His analysis of the contents of the present No. 1 follows. These are:

1. A continued article by Ackermann on the history of the Empiric sect after Galen's time. 2. The text of a Latin MS. of the pseudo-Hippocratic ivory capsule fragment (*De capsula eburnea aphorismi*) edited by Stoll. 3. A German version of chapters VII-XI of Galen's *De sanitate tuenda*, dealing with the hygiene of infancy, by Johann Karl Osterhausen. 4. Prolegomena for a biography of Maximilian Stoll, including a bibliography of his writings, edited by Wittwer. 5. Four letters on travels in France, England, Holland and Italy during 1787-8 by J. C. G. Schaeffer, Court Councillor and Body Physician to the Prince of Thurn und Taxis.

In this assemblage of titles, covering ancient medicine, pediatrics, biography, bibliography and physicians' travels, we have already a fair representation of the kind of material which Wittwer had in his mind's eye. In content and quality of material, his thin volume will compare favorably with any of its successors, from Henschels' *Janus* (1846-53) to Sudhoff's *Archiv* (1907-32). With this slender sheaf of worthwhile contributions, the periodical literature of the history of medicine may be said to have made a more respectable start than most.

F. H. Garrison.

# THE TREATMENT OF NEUROSYPHILIS*

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This discussion of neurosyphilis has for its goal object, a consideration of the prevention of the central nervous system manifestations of syphilis. It will be assumed that in syphilis, the central nervous system is usually invaded in the very early period of the disease, that in the majority of cases indications of this invasion are found through abnormalities of the cerebrospinal fluid, and that in many of the cases so involved, the usual routine treatment of syphilis is ineffective as far as central nervous system pathology is concerned. Evidence for these assumptions is to be found in many articles which have appeared in recent years. Our own experience has amply confirmed the hypothesis that routine treatment is not by any means entirely effective, whether this treatment is instituted in the very earliest stage of syphilis, or in the very late stage. Especially pertinent in this regard is the evidence presented by Moore of the cases of early syphilis showing the characteristically strong spinal fluid serology similar to what one finds in general paresis, which cases not only did not respond to vigorous anti-luetic treatment from the serological standpoint, but which developed definite late neurosyphilis.

Cases of neurosyphilis may be artifically divided into a number of groups on the basis of either clinical symptomatology, pathology, serological findings, or response to treatment. In a general way one will find that there is some correspondence between these different methods of classification, but there will be indeed many exceptions. The early cases, with very mild serological changes, usually fall into the group of meningeal disturbance, and many will respond quite well to various types of therapy. On the other hand, late cases, with strong serological abnormalities clinically represented by general paresis, having, from a pathological standpoint, an involvement of the true ner-

*Delivered before The New York Academy of Medicine, March 3, 1932.

vous elements, are much more difficult to treat satisfactorily. Between these two groups are many gradations and varieties.

From the standpoint of therapeutic results, one may well build up a hierarchy, from the simple meningeal cases to the most severe parenchymatous involvements, with gradations including the later meningo-vascular disorders and tabes dorsalis. It will be found, however, that there are many exceptions to the general rule of simply-evoked or more difficultly-obtained response to treatment.

In attempting to present the effectiveness of various therapeutic agents, one might begin therefore with the more simple cases and work up to the more severe. The other method of presentation, however, namely a consideration of the means that are most effective in the treatment of severe cases, and the application of the knowledge thus obtained to the more simple, is the plan of procedure of this presentation. The treatment of general paresis, then, will be the first consideration.

Let me emphasize at the beginning, that the type of treatment advocated for early systemic syphilis, that is, the routine treatment to be found in all text-book discussions on the subject, including courses of arsphenamin, bismuth, mercury, and iodid, have practically no value in the treatment of general paresis, nor does intraspinal therapy appreciably increase the effectiveness of the treatment.

In passing, it may be stated that very intensive arsphenamin treatment, combined with intraventricular, intracisternal, and intraspinal treatment, has some therapeutic value, but there are so many difficulties in the way of this type of treatment that it may be dismissed with only this mention.

The types of treatment that have been found most effective are, on the one hand, tryparsamide, and on the other hand, the febrile treatments. I shall not attempt to offer a careful analysis of the relative value of tryparsamide and fever treatment, nor shall I attempt to quote statistics to

show the exact percentage of satisfactory results obtainable. As a matter of fact, there are no satisfactory series of comparable cases treated by tryparsamide and fever respectively, hence any analysis that might be made would be extremely fallacious. I shall, therefore, have the temerity to make the rather dogmatic statement that the results of these two types of treatment are rather similar when considered from a percentage viewpoint. The literature is replete with statistics dealing with the results of malarial treatment, the series analyzed varying from a few cases to several thousands, and the final evaluation of successful results varying from approximately 25 per cent to 60 or 70 per cent, and indeed there are some statements that the treatment is hardly effective.

The inadequacy of all such statistics results from several causes, e. g., the criteria of improvement or arrest; the type of cases treated, that is, whether the material consists of rather early cases or whether it is made up of a majority of late, far-advanced cases; and finally, upon the amount of treatment given the patients.

Despite all these difficulties at arriving at any statistical conclusion, the average results of treatment are approximately as follows: 30 per cent of the cases treated make a good clinical-social recovery; another 30 or 40 per cent show definite evidences of some improvement as determined either by the clinical manifestations, serological results, or longevity.

As already stated, our own evidence indicates that the results with tryparsamide are quite similar to those obtained by febrile treatment. The most satisfying type of results is that in which the patient makes a clinical improvement so that there are left very little, if any, evidences in the psychological reactions of the patient of the in-roads of the disease, and in which there is, at the same time, a complete serological recovery. An example of this type of result obtained in one case by the use of tryparsamide, and in another case by malaria, will indicate to what I refer.

### Case 1

D.O. 30 Diagnosis: General Paresis
Symptoms: Euphoria, grandiosity—2 weeks
Blood Wass. positive 5/11/23
Sp. Fl. Wass. positive (0.05cc) Cells 36, Glob. 3+
Total protein Gold. 5555554322
Tryparsamide 114 Mercury 22
Blood Wass. negative 4/6/26
Sp. Fl. Wass. negative (1.0cc) Cells 4
Total protein 34, Gold. 0000000000

### Case 2

C.B. 44 Diagnosis: General Paresis
Symptoms: 1 year before treatment
Blood Wass. positive 8/2/27
Sp. Fl. Wass. positive (0.05cc) Cells 106, Glob. 3+
Total protein 77, Gold. 3453210000
Malaria 5 paroxysms (jaundice)
Tryparsamide 144
Blood Wass. negative 3/11/30
Sp. Fl. Wass. negative (1.0cc) Cells 4, Glob. 0
Total protein 46, Gold. 0000000000

A little less satisfying, but perfectly satisfactory by the criterion of practical results, is the type of case in which there is a thoroughly good clinical-social recovery without serological improvement. The following cases exemplify this type of result.

### Case 3

D.R. 40 Diagnosis: General Paresis
Symptoms: Personality change, deterioration.
Blood Wass. positive 2/2/26
Sp. Fl. Wass. positive (0.2cc) Cells 12, Glob. 2+
Total protein 80, Gold. 5544311000
Tryparsamide 134
Blood Wass. negative
Sp. Fl. Wass. positive (0.4cc) Cells 16, Glob. 1+
Total protein 47, Gold. 4454200000
Clinically well

### Case 4

W.C. 59 Diagnosis: General Paresis
Symptoms: Eight months duration, speech defect, "dementia."
Blood Wass. positive 5/5/25
Sp. Fl. Wass. positive (0.1cc) Cells 8, Glob. 2+
Total protein 75, Gold. 5555432100

Malaria 14 paroxysms — Tryparsamide 162
Arsphenamin 19 — Bismuth 41
Blood Wass. positive 9/22/31
Sp. Fl. Wass. positive (0.4cc) — Cells 4, Glob. 1
Total protein 48, Gold. 5543200000
Clinically well.

It is my impression that this type of result is less satisfactory because of the greater probability of relapse. There may be some question about this statement, but it is a matter that needs further study.

Much less satisfying, from the human standpoint, but just as important from the point of view of theory and knowledge of the subject, is the type of case in which no satisfying result measured by the psychological status of the patient is obtained, but in which there is a serological cure and evidence of an arrest of the disease. We have many examples of this type of case in which the patient does not make a clinical improvement in regard to his social reactions, or to his mentality, but in which the physical condition remains excellent over a period of years, and in which there is a complete serological cure.

The maximum of clinical results, whatever they may be, are usually obtainable in the course of two, or three, or four months. On the other hand, the serological results always take a very much longer time. In fact, in many cases, a period of three, four, or five or more years are required for a serological cure. In some cases the serological recovery is relatively prompt, and a complete serological cure is obtained in the course of a year. These are in contrast to the majority of cases where, if serological cure results at all, it comes about only after several years. The reason for this difference is another of the problems of treatment that is very obscure, and which it is hoped that future studies will elucidate.

I have stated that it is my opinion that the effectiveness of tryparsamide and fever, from the statistical standpoint, is very similar. This does not mean, however, that in a given case one treatment is as effective as the other. I

have no doubt that in some cases fever therapy will bring better results than tryparsamide, and vice versa. It is, of course, impossible to have pure experiments to prove this contention. However, we have many illustrations of cases that have not done well with one type of therapy, and when the other is given, improvement ensues. The following case illustrates the effectiveness of malaria after a relative failure with tryparsamide.

### Case 5

K.B. Diagnosis: Taboparesis
Symptoms: Excitement.
Blood Wass. positive 1/16/23
Sp. Fl. Wass. positive (0.05cc) Cells 28, Glob. 4+
Total protein Gold. 5555555430
Arsphenamin 42 Tryparsamide 86 Mercury 28
Blood Wass. positive
Sp. Fl. Wass. positive (0.1cc) Cells 18, Glob. 2+
Total protein 38, Gold. 5553300000
Malaria 14 paroxysms Tryparsamide 100
Blood Wass. negative 8/2/30
Sp. Fl. Wass. negative (1.0cc) Cells 0, Glob. 1+
Total protein 22, Gold. 2111000000

There are cases in which either a variation or combination of treatment, or the repetition of treatment will produce success out of what appears to have been failure, as shown by the following case.

### Case 6

B.E 29 Diagnosis: General Paresis
Symptoms: Depression
Blood Wass. positive 9/30/24
Sp. Fl. Wass. positive (0.1cc) Cells 225, Glob. 2+
Total protein Gold. 5555531000
Tryparsamide 91
Clinical relapse
Blood Wass. positive 9/4/28
Sp. Fl. Wass. positive (0.05cc) Cells 70, Glob. 3+
Total protein 103, Gold. 5554310000
Malaria 10 paroxysms Tryparsamide 18
Typhoid vaccine fevers 9 Bismuth 25
Blood Wass. positive
Sp. Fl. Wass. negative (1.0cc) Cells 0, Glob. 1+
Total protein 40, Gold. 1110000000
Clinically well.

The foregoing indicates the complexity of the problem of the most adequate form of treatment for a given individual. Unfortunately, the limitations of time and space are such that this matter cannot be here discussed. I would merely pause to state that we are only at the beginning of our study of the best and most effective forms of treatment.

Let me now sum up in a didactic fashion my personal viewpoint of the treatment of general paresis. Results that are eminently satisfying are obtainable in 30 per cent or better of the cases of general paresis as we see them in the clinic and in private practice. The actual therapeutic attack may be made by tryparsamide or fever alone, but I believe unquestionably the most satisfactory results are obtained by a combination of these methods. It is perfectly feasible to start the patient with tryparsamide, which is the simplest satisfactory treatment available. If, after two or three months of treatment, the results are not what one wishes, then one may supplement the tryparsamide by fever, or if one begins at the outset by fever therapy, it is advantageous to continue the patient on tryparsamide until there is a complete serological cure. Fever may be produced therapeutically by malaria, typhoid vaccine, diathermy, or radio-thermy. One must again confess that there is no body of information that will allow one to draw hard and fast rules as to which is the most effective. Again, turning to personal experience, it is my belief that the typhoid vaccine is the least effective. I have had no personal experience with radio-thermy, nor is there enough experience as expressed in the literature, to allow one to draw any conclusion. My own experience with diathermy is not sufficient to allow of any dogmatic statement, but from what experience I have had, and from what literature there is, it seems a fair conclusion that it is equally as effective as malaria.

Next in order of difficulty of obtaining therapeutic results are the tabetic cases. A limited number of cases of tabes dorsalis respond very well to long-continued use of

arsphenamin, but in the majority this type of treatment is not reasonably successful. In this group of cases, intraspinal therapy unquestionably has a very high degree of effectiveness. There are, however, many objections to this method of treatment, among which may be mentioned the discomfort to the patient, the difficulty of the procedure limiting it to the use of a few specialists or clinics, the possibility of damage to the spinal cord, and the practical difficulty of getting the patient to submit to a sufficient number of treatments. Tryparsamide overcomes a great many of these objections and therefore, if as effective therapeutically, is far more satisfactory. The evidence at hand indicates that it is at least as effective therapeutically as the intraspinal treatment. Certainly, by the use of tryparsamide, aided at times by arsephenamin and bismuth, one is able to obtain a serological cure in almost every case of tabes. The time required, however, for this result varies tremendously. On the one end of the series one finds the cases that obtain a serological cure within a few months, and at the other end are the cases which take years, if the result is obtained at all. This difference in the result of treatment may be illustrated by two cases.

### Case 7

J.M. 52 Diagnosis: Tabes
Blood Wass. negative 6/19/23
Sp. Fl. Wass. positive (0.05cc) Cells 10, Glob. 3+
Gold. 5555553200

Tryparsamide 85
Blood Wass. negative
Sp. Fl. Wass. negative (1.0cc) Cells 3, Glob. 1
Total protein 28, Gold. 0000000000

### Case 8

J.O. 53 Diagnosis: Tabes
Blood Wass. positive
Sp. Fl. Wass. positive (0.1cc) Cells 74, Glob. 2+
Total protein 59, Gold. 3442100000
Tryparsamide 180 Arsphenamin 8 Intraspinal 1
Blood Wass. doubtful
Sp. Fl. Wass. negative (1.0cc) Cells 2, Glob. 1+
Total protein 34, Gold. 5532100000

The clinical results vary almost as much as the serological results. There are certain cases in which a very few injections of tryparsamide will free of lightning pains, crises, and the like, and improve the general condition and allow for considerable improvement in the ataxia in a very short period. In other cases, the improvement will ensue only after many months of treatment. Whereas, on the other hand, there are cases which seem to do badly both in general physical health and as regards the rapidity of progress of the ataxia and increase in pains.

Even more disturbing to our intellectual attitude about the treatment are the cases which show relatively prompt serological cures, but in which the symptoms are unabated. Thus, there are cases in which, despite serological cure, gastric crises continue with their previous regularity, and severity. We see cases which in spite of the serological cure, go on to the development of the destructive joint changes characteristic of the so-called "Charcot joints."

Once more we must take refuge from a discussion of the reasons for these failures, in the limitation of time and space.

The next question is whether fever is more or less effective in handling the tabetic problem. The literature indicates that malarial therapy is not as effective in tabes dorsalis as in general paresis. Our own experience, which I fear is not wide enough to allow one to attempt to overthrow the more extended reports found in the literature, nevertheless inclines me to the belief that fever is extremely effective in many cases of tabes, especially from the clinical viewpoint. This may be illustrated by the following case.

### CASE 9

J.M. Diagnosis: Tabes, Gastric crises
Blood Wass. negative 6/29/25
Sp. Fl. Wass. positive Cells 66, Glob. 2+
Gold. 4443200000
Tryparsamide 60 Intraspinal 2
No relief of symptoms
Blood Wass. negative

Sp. Fl. Wass. negative (1.0cc) Cells 2, Glob. 1+
Total protein 27, Gold. 2200000000
Malaria 18 paroxysms
Blood Wass. negative
Sp. Fl. Wass. negative (1.0cc) Cells 0, Glob. 1+
Total protein 33, Gold. 0000000000
Patient symptom-free.

I may sum up my experience in the treatment of tabes as follows. At the present time tryparsamide would seem to be the best method of treating the majority of cases. Where this is not sufficiently effective, or where there are contra-indications, intraspinal therapy has a high potency, and one has a considerable degree of hope in the effectiveness of fever for those cases which have not responded satisfactorily to tryparsamide. A great majority of cases, therefore, may be expected to show both clinical improvement and serological cure. At least, an arrest of the progress may be usually expected although there is an occasional exception to this rule.

The treatment of the meningeal type of neurosyphilis is, on the whole, simple and satisfying. In both the early and late varieties of this disorder, tryparsamide may be expected to give a serological cure in almost every case. In this variety of disorder, tryparsamide acts almost, if not entirely, as a specific drug. In the majority of instances, clinical improvement is very prompt and serological cure usually occurs within the first year. There are cases, however, in which prolonged treatment may be required to get the serological effect. Once more we present two cases to illustrate the variation in time factor in obtaining serological results.

### Case 10

E.E. 30 Diagnosis: Meningovascular neurosyphilis, (extra-ocular palsy)
Blood Wass. positive 10/16/26
Sp. Fl. Wass. positive Cells 440, Glob 3+
Total protein 85, Gold. 5553210000
Tryparsamide 43
Blood Wass. negative 10/26/27
Sp. Fl. Wass. negative (1.0cc) Cells 0, Glob. 1+
Total protein 43, Gold. 2211000000

### CASE 11

R.F. Diagnosis: Meningovascular neurosyphilis.
Blood Wass. negative 4/3/25
Sp. Fl. Wass. positive Cells 44, Glob. 2+
Total protein 333, Gold. 0001144321

Tryparsamide 90
Blood Wass. negative 5/3/30
Sp. Fl. Wass. positive (1.0cc) Cells 4, Glob. 1+
Total protein 70, Gold. 1110000000

Fever treatment is rarely, if ever, required in this variety of neurosyphilis. In fact, in our experience, it has not been necessary to resort to this form of treatment, and therefore I have no personal experience with its effectiveness. That it is effective, however, would be expected from logical reasoning based on the experience with other types of neurosyphilis, and this is verified by the experience as reported in the literature on the subject.

No consideration will be given to the pure vascular types of neurosyphilis because this will widen the field too greatly, and presents an entirely different subject, the subject of vascular syphilis in which the central nervous system damage is merely incidental to a disease of the blood vessels.

There are several other variations of clinical and pathological effects of syphilis on the nervous system, the treatment of which we must also avoid at this time.

The logical conclusion which would seem to flow out of what has been said up to this point is that with tryparsamide and fever therapy at our disposal, the majority of cases of syphilis of the central nervous system can be effectively handled, if not from the standpoint of rehabilitation yet from the theoretical standpoint of a slowing up of the process and a serological improvement or cure. The great handicap, from the standpoint of satisfactory clinical results, is that the patients, when obtained for treatment, are so far advanced in the disease in many instances, with so much damage to the nervous system, that the most that can be expected is a partial restitution of the individual as a functioning organism.

Fortunately the diagnosis of neurosyphilis is practically quite simple through the examination of the cerebrospinal fluid. As has already been said, the majority of cases that develop the severe nervous system lesions show abnormalities in the cerebrospinal fluid from the very early stages of syphilis. It is therefore only necessary to follow adequately the cerebrospinal fluid in the course of syphilis in order to have an index in the first place as to the potential probabilities of nervous system damage, and secondly, as to the effectiveness of the type of treatment used. I have already stated that in many cases, arsphenamin, bismuth, and mercury do not effectively hinder the progress of syphilis in the nervous system. Perhaps two cases, one of early, and one of late syphilis, developing neurosyphilis while under arsphenamin therapy, may be used as evidence for this statement.

### Case 12

D.G. Diagnosis: Primary Syphilis Meningeal neurosyphilis
Primary sore March, 1930. Blood Wass. positive
Neo-arsphenamin 15 Bismuth 9
Blood Wass. negative 9/30/30
Sp. Fl. Wass. negative Cells 0, Glob. 0
Total protein 48, Gold. 0000000000
Severe headaches
Bismuth 7 Neo-arsphenamin 2 Silver arsphenamin 8
Blood Wass. positive 5/7/31
Sp. Fl. Wass. negative Cells 204, Glob. 1+
Total protein 150, Gold. 4555555554
Clinical cure with tryparsamide

### Case 13

W.M. 36 Diagnosis: Latent Syphilis
Symptom-free
Blood Wass. positive 10/24/27
Sp. Fl. Wass. negative (1.0cc) Cells 0, Glob. ?
Gold. 0000000000
Neo-arsphenamin 39 Bismuth 13
Blood Wass. positive 9/14/29
Sp. Fl. Wass. positive Cells 56, Glob. 3+
Total protein 100, Gold. 5555555300
Speech defect, unequal pupils, mental confusion
Tryparsamide 98 Bismuth 71
Blood Wass. negative 10/24/31
Sp. Fl. Wass. negative (1.0cc) Cells 45, Glob. 1+
Clinically well Total protein 27, Gold. 5555310000

In both these cases tryparsamide produced a successful clinical result.

By this devious route, we have finally reached the point which I set out to make at the beginning of this paper, namely, that prevention of the devastating effects of syphilis upon the nervous system is theoretically possible, and that practically it can be obtained with the methods now available in nearly every case. Having shown the effectiveness of our therapeutic agents in halting the progress, in various types of neurosyphilis even after the in-roads have been great and the foothold of the spirochetes firmly established, we are in a position to maintain the thesis that if similar treatment were instituted much earlier, arrest of the progress could be much earlier obtained, and the damage minimized, if not entirely avoided.

In my concluding remarks, I would like to emphasize that syphilis is a serious disease because of its effects upon two great systems, the cardiovascular system, and the nervous system. The other effects of syphilis are much less important, much less serious, and much more amenable to simple antiluetic therapy. From our standpoint, therefore, it is of the utmost importance that every case of syphilis should be considered as to its actual or potential involvement of the nervous system. This means a careful neurological survey of the infected patient from the very earliest to the latest period of the disease, and this clinical consideration must be checked by examination of the cerebrospinal fluid. When the cerebrospinal fluid is found to show changes characteristic of central nervous system invasion, the effect of treatment on the spinal fluid serology must be given first place in the future treatment. If this is done in the early stages of syphilis and it is found that the type of treatment given does not produce serological improvement, it then becomes necessary to change to the treatment that will be found effective. This means, specifically, that where arsphenamin, bismuth, and mercury, are found to be ineffective in producing serological cure,

one must turn either to tryparsamide, or fever therapy, or a combination of the two, and if this principle of treatment is adhered to, there is, in my opinion, ample evidence to make one believe that the central nervous system involvement may be eradicated or at least held in check.

# CARDIOVASCULAR SYPHILIS*

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Our knowledge of the behavior of syphilis in the cardiovascular system has passed through interesting stages in its development. The first stage was that of discovery. To Morgagni, in 1761, goes the credit of clearly recognizing the relation between syphilis and aortic aneurysm. The next definite step was taken by Ricord in 1845, when he gave us the earliest description of syphilis of the heart. He described a gumma of the myocardium. Then our own Dr. Welch, in 1876, added to the picture that of syphilitic aortitis; and Döhle, in 1885, first made clear and insisted upon the relation between syphilis and lesions of the aorta. The final step in the stage of discovery was taken by Reuter, in 1906, when he demonstrated the treponema pallidum in the wall of the aorta in syphilitic aortitis.

The next stage in our knowledge is that in which the facts that had been obtained from postmortem material were applied to the diagnosis of syphilis of the heart in the living. This only began in 1906, after the discovery of the Wassermann reaction. Longcope[1], in 1913, painted a very clear picture of the diagnosis and treatment of syphilitic aortitis, and Brooks[2], in the same year, laid strong emphasis upon involvement of the myocardium, both in the secondary and tertiary stages of the disease. Warthin[3], in 1917, attracted further attention to the myocardial lesions of syphilis.

Now it is possible that we are entering upon a third stage in our knowledge of syphilis of the cardiovascular system. Syphilis has been fairly adequately treated for the past fifteen years. Much of the fundamental work has been done in the pathology and the clinical diagnosis of the condition. Nevertheless, we know very little about

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such important points as the time when aortitis begins to be manifest, the efficacy of early treatment in preventing cardiovascular involvement and the influence of treatment upon the course of the disease. With our recent development of the statistical method of study of large numbers of patients, over long periods of time, and with our highly developed system of follow-up, is it not possible that we are on the way toward providing an answer to many of these important questions in the natural history of the disease?

It is obviously not possible nor desirable to give, within the limits of this paper, a formal presentation of the entire subject of cardiovascular syphilis. Instead, an attempt will be made to paint a picture of the disease as a whole based upon the fundamental work that has been done in the past and, at the same time, to call attention again to the great gaps in our knowledge that make this picture incomplete. In the past, our thinking has been hampered by the habit of considering the various manifestations of syphilis of the cardiovascular system as separate disease entities. We have been drilled in the symptoms and signs of aneurysm, of aortitis, or of aortic insufficiency, and some of us have lost sight of the fact that they are only different manifestations of the development of the same pathologic process.

To begin at the beginning, in what manner does the spirochete reach the cardiovascular system? From the chancre, the organisms invade the blood stream and the lymphatics, pass through the right heart and into the lungs. Here those that do not pass through into the pulmonary veins and thence back into the heart and the general circulation are carried by the pulmonary lymphatics into the tracheo-bronchial lymph nodes. From here they are thought to pass by retrograde lymphatic flow into the tissues of the mediastinum and into the perivascular lymph spaces about the vasa vasorum in the adventitia of the aorta. Martland[4] has offered an ingenious explanation of the relative rarity of congenital syphilis of the heart and aorta. He has pointed out that in utero the pulmonary

circulation is small and that, therefore, only a small number of spirochetes are carried to the lung and thence to the tracheo-bronchial lymph nodes and aorta.

Now let us look for a moment at this matter of congenital syphilis. McCulloch[5] suggests that infants that are still born or die before aged two, correspond to the group of adults with generalized syphilitic invasion, the secondary stage. At postmortem, the myocardium shows evidence of syphilitic involvement with fibrosis and round cell infiltration. Spirochetes are often demonstrated, more frequently in the myocardium, but also in the aorta. The children that survive this period of invasion have either temporarily or permanently overcome their infection. Some of them, in later life, will develop syphilitic aortitis or myocardial gummata. Lamb[6] states that aortitis has been reported at ages twelve, seventeen and nineteen. On the other hand, careful clinical studies by Matusoff and White[7], McCulloch[5], Givan[8], Previtali[9], and others, have uniformly failed to show any demonstrable clinical signs of syphilitic heart disease in congenital syphilitics that survive. Is it not possible that in congenital syphilis, as in acquired syphilis, there is a long latent period from the time of infection to the onset of clinical signs and symptoms? To answer this very important question, we need more studies on older congenital syphilitics, and we need to keep them under observation, if possible, until death. To my knowledge, no such study has been made. Thus, to recapitulate, is it not possible that congenital syphilitics that are still born or that die during early infancy are in the period of invasion of the spirochetes which have come by way of the blood stream and invade the myocardium? If the individual survives, these organisms have been removed by phagocytosis, making myocardial lesions uncommon in those that outlive this period. The spirochetes that have been caught in the mediastinal lymph nodes, however, may reach the perivascular lymph spaces of the vasa vasorum in the aorta and initiate the lesions of aortitis. This condition we should expect to discover from fifteen to twenty years later.

Now let us turn our attention to some of the problems of the cardiovascular system in acquired syphilis. In this discussion, no attempt will be made to catalogue all the symptoms and physical signs of aortitis, aortic insufficiency and aneurysm, because they are too well known and have been ably recounted by others. Instead, let us think of syphilis of the cardiovascular system as a whole, and let us discuss some of its special problems. In the first place, why is it that the diagnosis is rarely made until twenty years after the primary lesion was acquired? Of course, one obvious explanation presents itself; the patient usually does not come for examination of the cardiovascular system until he is aware that something is amiss. Unfortunately, he does not reach this state until twenty years have elapsed since the chancre. It is generally agreed that infection of the heart and aorta takes place during the secondary stage of syphilis. The spirochetes probably lie inactive between the muscle bundles or in the perivascular lymph spaces and the vast majority are removed by phagocytosis. The remainder lie dormant for years, causing little or no tissue reaction. Fordyce[10] has suggested that allergy may offer an explanation for this phenomenon. The tissues may slowly become sensitized to the spirochetes so that, whereas in the beginning they did not react to the presence of these organisms, in the end, after several years, they react with edema, round cell infiltration and destruction of tissue, resulting in the development of recognizable clinical symptoms.

Some of the early writers have told us that a diagnosis of involvement of the heart can be made during the secondary stage of the disease. They point to palpitation, shortness of breath, tachycardia, bradycardia, premature beats and the development of apical systolic murmurs as evidence that this has occurred. They feel that the diagnosis is strengthened when these symptoms and signs clear up promptly under antiluetic treatment. More recently, workers who have studied cases of primary and secondary syphilis have failed to find definite evidence of involvement of the heart or aorta. The electrocardiogram and the x-ray

have shown no changes[11], and the symptoms and physical signs have been considered too indefinite to make a positive diagnosis. Clearly, the two views are diametrically opposed, and in order to arrive at a final conclusion, it will be necessary to study a large series of young syphilitics in the primary and secondary stages with all the means of cardiovascular examination at our disposal, and to employ very rigid criteria.

In the present state of our knowledge, what are the earliest recognizable symptoms of syphilitic heart disease? It will be remembered that the earliest lesions are in the arch of the aorta, above the semilunar valves. Aortic insufficiency, aneurysm and syphilitic coronary disease are late lesions. Therefore, we must try to diagnose syphilitic aortitis before these sequelæ have appeared. Lamb[6] found in his series of 26 cases of uncomplicated aortitis that eleven, or nearly half, had no symptoms whatsoever. Those that did have symptoms complained first either of substernal pain or paroxysmal dyspnea. The substernal pain was present most of the time but aggravated by exertion or emotion. He states that autopsy has shown that this symptom is not necessarily connected with changes in the coronary arteries.

White[12] states that aortitis itself may be symptomless, but that sometimes there is a more or less constant dull ache high up under the sternum. With our greater familiarity with the pain of coronary disease today, is it not possible that critical studies may be able to separate the early cases of aortitis from the more advanced, in which the mouths of the coronary arteries have become involved in the syphilitic process? Carter[13] calls attention to another early symptom; the abrupt onset of dyspnea on exertion, with slight edema. Thus, to help us in the early diagnosis of syphilitic aortitis, we have substernal distress or aching, paroxysmal dyspnea, often nocturnal, and the abrupt onset of shortness of breath on exertion. In addition, if we find a systolic murmur at the aortic area, a hollow ringing aortic second sound, in the absence of hypertension, evi-

dence in the teleoroentgenogram of a widened aorta, and a history of syphilis or a positive Wassermann reaction, the diagnosis of syphilis of the aorta has been made.

Now let us turn to the problem of syphilis of the myocardium. Gummata of the myocardium have been described since our earliest knowledge of syphilis of the heart. Their incidence is not very high but they are occasionally the cause of sudden and unexpected death. They are primarily vascular in origin, in that they begin as areas of round cell infiltration and necrosis about one of the branches of a coronary artery. True syphilitic myocarditis with diffuse infiltration of plasma cells between the muscle bundles, and parenchymatous degeneration of the muscle fibres, is a much rarer lesion, however. Warthin[14], in the course of his writings, has laid more and more stress upon chronic and acute syphilitic myocarditis. He states that the important, if not predominating, rôle played by syphilis in myocardial incompetency is not being recognized. His work, however, has not been confirmed by other careful students. It has, however, resulted in a tendency to overemphasize the myocardial lesions and thus distract attention from the aorta. Carter and Baker[13] found the myocardium alone involved in relatively few cases after gummata have been excluded. White [12] states that cardiovascular syphilis consists, therefore, primarily of luetic aortitis, infrequently it means myocardial disease. To recapitulate then, there is definite proof that myocardial gummata occur occasionally, but the existence of a true diffuse syphilitic myocarditis in acquired syphilis needs further postmortem proof.

Now what are the criteria for the diagnosis of syphilis of the myocardium? Given an unusual enlargement of the heart without demonstrable cause, a diffuse apex thrust without murmurs and with a poor first sound at the apex and a low systolic blood pressure in a patient with a positive Wassermann reaction and Carter[13] states that syphilitic involvement of the myocardium should be suspected. We

have seen one patient that fulfilled all these criteria and autopsy showed a large gumma in the myocardium.

Now before we discuss the treatment of cardiovascular syphilis, it is well for us to have in mind a clear picture of the morbid processes we are attempting to influence. In the first place, we know that the average duration of the disease from the chancre to the first diagnosis of cardiovascular syphilis is twenty years[15]. Again we know that the average period from the chancre to death is twenty-three years[15]. We remember the extensive changes that have taken place in the wall of the aorta, in an aneurysm, or in the aortic valves, in aortic insufficiency before a clinical diagnosis is usually made. Because of these facts, we approach the problem of treatment in true humility of spirit. When we begin treatment, the disease is already far advanced, and in spite of our best efforts, death comes on apace and the postmortem often shows a surprising amount of aortitis, in spite of so-called thorough treatment.

Gager[16] has recently called attention to some observations upon the comparative incidence of cardiovascular lesions in syphilis before and since the salvarsan era. Langer found syphilis in 4.02 per cent of necropsies in Virchow's Krankenhaus in 1906-07, and 4.32 per cent in 1925. However, the incidence of aortitis was 33.3 per cent in the first group before the salvarsan era and 83.87 per cent in 1925. Heller found that the number of aneurysms had quadrupled since salvarsan. Schlesinger showed that the time interval from the chancre to death was 23.4 years in untreated cases, 22.1 years in partially treated, and 15 years in the well treated. Whether these figures will be borne out by similar studies in this country remains to be seen. Nevertheless, they make us pause before we advocate vigorous antisyphilitic treatment for cardiovascular lues. The plans advocated by White[12], Carter[13], Lamb[6] and many others are similar in that they are all conservative and limit the use of neosalvarsan to small doses. It is agreed that antiluetic treatment should be omitted during periods of congestive failure and that when given, it should be in carefully plan-

ned courses with definite rest periods. The following plan is offered as one that has proven reasonably satisfactory in our hands. Treatment is begun with a course of mercury salicylate 0.03-0.06 gm. intramuscularly, once a week, for six weeks. At the same time, potassium iodide up to gms. 2, three times a day is given. Then a rest period of two months is allowed followed by a course of potassium bismuth tartrate 0.1-0.2 gm. intramuscularly until 2 gms. have been given, provided no toxic symptoms appear. After another rest period of two months, a course of six injections of neosalvarsan may be given, beginning with 0.1 gm. and increasing up to 0.45 gm. at weekly intervals. This plan of treatment will occupy about one year and should be continued for a second year and modified to suit the needs of the individual case. It is not often that one obtains a permanently negative Wassermann in these patients and, therefore, not the Wassermann reaction but the clinical condition of the patient should be the guide for treatment. The greatest danger is in overtreating these patients. If after a reasonable course of treatment they are doing well, they had best be left alone and kept under observation. It has been conclusively shown that the average duration of life from diagnosis of cardiovascular syphilis to death is from two to three years. A much larger series of carefully treated cases than have been reported so far is needed to show that this life expectancy can be increased. The hope for the future in the prevention of cardiovascular syphilis depends upon measures to prevent syphilis itself. Whether thorough treatment of the primary stages will prevent later involvement of the heart and aorta, it remains for further studies to show.

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# THE PATHOLOGY OF SYPHILIS*

## With Special Reference to the Development of Luetic Aortitis

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The pathology of syphilis of the circulatory and nervous systems will be discussed from the viewpoint of a general pathologist, outlining the anatomical pathways of infection in acquired syphilis.

Most of the facts herein stated are generally accepted by recent authorities and are based upon clinical, pathological and experimental evidence.**

I shall draw from these some deductions and conclusions which may point the way to further research into, and increased understanding of this disease.

### Inoculation and Primary Incubation Period

The treponema pallidum is usually deposited on an abrasion on the genitals. An abrasion is, however, not necessary and it may often be microscopic.

The spirochetes on account of their motility and also probably due to the capillary attraction of the open lymph-spaces are carried deep into the initial site of inoculation and there is a rapid reproduction of the organisms in the lymph-spaces and perivascular lymphatics.

Many pass rapidly into the capillaries and reach the important viscera within two to three days after inoculation. Hence, so-called abortive excisions of the chancre and abortive injections of arsphenamines, etc., will not prevent the development of syphilis.

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**In preparing this sketch, I have quoted extensively from the writings of Stokes, with whose views I am in entire accord.

Syphilis is, therefore, a systemic general infection days and even weeks before the appearance of the chancre.[1]

The greater number of the rapidly reproducing spirochetes, however, enter the surrounding lymphatics and drainage on the slower lymphatic stream to the regional lymph-nodes begins.

### Primary Stage—Chancre

As the rapidly growing spirochetes increase in number, the endothelial cells of the capillaries swell and an obliterating endarteritis occurs. Many new capillaries are formed. Perivascular collections of lymphocytes and plasma cells appear at an enormous rate and a papule with induration results. The typical Hunterian chancre, a local defense reaction at the site of inoculation, is formed.

Spirochetes rapidly reproduce and the initial sore teems with organisms. The direct feeding of the blood stream continues and increases, producing a bacteremia. Multiple, metastatic foci develop throughout the body. Their number, location and activity are proportional to the virulence of the organisms and the host.

The feeding of the slow lymphatic stream increases. Spirochetes reach the regional lymph-glands. Many are killed by the phagocytic activity of the reticuloendothelium of these nodes but some always survive and pass these defensive reservoirs and eventually reach the blood through the lymphatic duct, etc., or remain locked up in the lymph-nodes, to reinfect the lymph-stream or blood years after.

Clinically, during this stage, the chancre develops with wide variations in size and appearance. The local lymphadenitis develops with satellite bubo. Systemic symptoms, such as headache, pains in bones, etc., are frequent and even occur before the chancre. The blood begins to show a positive Wassermann reaction.

### Early Secondary Stage

The chancre now heals with the production usually of a tell-tale scar. Spirochetes become fragmented and scant.

Lymphocytes and plasma cells disappear and fibrosis takes place.

The remaining organisms are usually completely destroyed or they may become locked up in the fibrous scar and form the nidus of a chancre redux.

Many of the early metastatic foci are now healing, in a manner exactly similar to the healing of the chancre. Local immunological reactions undoubtedly play an important rôle.

The marked bacteremia from the chancre and early secondary foci causes countless secondary infections of the skin, bones and important viscera. In these areas of infection a rapid reproduction of spirochetes takes place followed by a characteristic cellular reaction, similar in every respect to that of the original chancre, with consequent formation of innumerable secondary lesions.

Clinically, the secondary rash appears. Macular, if the predominant feature is the formation of new capillaries, and papular if the perivascular collections of lymphocytes and plasma cells are marked.

A generalized lymphadenitis occurs, due chiefly to lymphatic drainage from the innumerable lesions of the skin and mucous membranes. Enlargement of the spleen is common. Bone and nervous lesions begin. Special structures, as the eye, ear, liver and kidneys may be affected with serious results. A positive Wassermann reaction develops with the refractory state.

### Late Secondary Stage

Systemic defense, with the production of agglutinins, lysins, etc., now comes into play. Systemic resistance reaches its highest point converting the disease into latent syphilis.

Secondary foci in all stages of activity and decline occur all over the body. Healing occurs by fibrosis. Most of the spirochetes are destroyed. Sterilization, however, is never

complete and provides bases for relapses, which are so characteristic of all stages of syphilis.

Spirochetes disappear from the blood, or occur in occasional showers.

In no stage of syphilis do the spirochetes multiply in the circulating blood to any appreciable extent.

Parenchymatous tissues, such as the lungs, heart muscle and liver, rid themselves of spirochetes by drainage into the regional lymphatics and lymph-nodes.

The spirochetes enter the perivascular lymphatics, the lymph-node reservoirs and inaccessible parts of the bones and nervous system, where they cannot be reached by the circulation. Here they rest, or reproduce in the quiet, mild, anaerobic lymph. *Syphilis now becomes a disease of the lymphatics and ceases to be a blood disease,* except for occasional showers of spirochetes, usually scant in number, which may be thrown into the blood stream due to the reawakening of old microscopic foci.

Clinically, in this stage, the secondaries disappear spontaneously. Systemic manifestations subside. The only clinical evidence remaining being a palpable spleen and liver and asymptomatic neurosyphilis.

Due to defects in resistance or revival of the partly extinguished foci, any lesion in primary or secondary stage may reappear, especially those on the mucous membranes.

### Infection and Drainage of Certain Viscera

The mode of infection by the blood stream and the manner of the riddance of spirochetes from some of the viscera in the early and late secondary stage is of great importance, and must be considered in more detail.

### The Lungs

In the stage of bacteremia when the chancre is feeding the blood stream with innumerable spirochetes, the lungs are the first important organs to receive the dosage of or-

ganisms. In fact, on account of their very great capillary area, they receive a greater dosage than perhaps any other part of the body, with the exception of the skin.

The lungs are the most important and extensive capillary filtering bed of the venous circulation for large sized particles.

Let us take for example, a case of septic endometritis, complicated by a thrombophlebitis of an ovarian vein. Constant showers of hemolytic streptococci, mixed with blood platelets, fibrin, polymorphonuclears and agglutinated cocci enter the inferior vena cava, pass rapidly through the right side of the heart and enter the lungs. Most of the streptococci are filtered out or retained in the lungs and multiple, symmetrical, bilateral, hematogenous, embolic abscesses occur. Infection of the pleura by continuity, or by rupture of a surface abscess, with the production of an empyema often ensues. The lungs in such cases show a remarkable ability to rid the blood stream of the infection. Sometimes the patient may even recover. If she dies, there may be little evidence of systemic emboli.

In the bacteremia in the second stage of syphilis, however, the spirochetes are unaccompanied by large size particles, such as agglutinated bacteria, etc., and it is reasonable to suppose that most of the spirochetes easily pass through the lung capillaries and enter the systemic circulation.

Many, however, are undoubtedly slowed in the lung capillaries, cling to the side of the vessel walls and, because the treponema pallidum are always attempting to leave the circulation for extravascular tissues, in which they are less liable to injury, penetrate into the interstitial portions of the lung.

Those that do penetrate the lung parenchyma, in their attempt to get far away from the blood stream, will not under ordinary circumstances remain there for any length of time. First, they do not like the proximity to oxygen; second, many will be phagocyted by the alveolar epithe-

lium, which is mesothelial in origin and a part of the reticuloendothelium; finally, and what is more important, the spirochetes will be taken up rapidly by the lymphatics and drain into the hilus nodes, due to the great drainage power of the lungs in ridding themselves of foreign and undesirable particles.

A similar process is seen in the handling by the lungs of the tubercle bacillus, in the storage of coal pigment and silica in the hilus nodes and in the remakable lymphatic drainage seen in malignancy of the lung.

The lungs eventually rid themselves of the spirochetes by way of their lymphatics, which drain to the peribronchial and regional nodes of the mediastinum. These become collecting stations, or reservoirs, for the storage of spirochetes. Here they are exposed to the phagocytic action of the reticuloendothelial cells of the lymph-sinuses.

I am of the opinion that the above conception explains the rarity of pulmonary syphilis. It is a notable fact that in acquired syphilis, gummata of the lungs are unusual. The various forms of pulmonary syphilis described by clinicians and roentgenologists and seldom substantiated at autopsy, have usually been of the hilus type. A diffuse, fibrotic infiltration forms a doubtful and nebulous pathological entity.

Furthermore, it is of interest to note, that the only common form of lung syphilis is that seen in stillborn infants, or in those who live only a few days, in which the well known "pneumonia alba" is encountered. Microscopic examination of these lungs show chiefly an arrested development rather than an active inflammation, with considerable cellular fibrous tissue about the blood vessels.

In heredosyphilis the child is infected through the placenta, and an incalculable number of spirochetes circulate throughout most of the organs, the number having no parallel in acquired syphilis. The rarity of heart disease in congenital syphilis might be explained, therefore, by the fact that the lungs of the fetus have escaped the large

dosage of spirochetes, because the fetal circulation does not pass through them to any great extent.

In instances in which the lungs receive an unusual dose, a fatal pneumonia alba occurs, principally because the lungs are not aereated and offer a more favorable soil for the reproduction of spirochetes than do the adult, oxygen containing, lungs.

### The Heart

In the septicemia stage, spirochetes undoubtedly reach the heart muscle in considerable numbers by way of the coronary circulation.

Does syphilis of the heart muscle begin in this stage?

Warthin's[2] observations led him to conclude that in the second stage of syphilis there is a very active specific infiltration of the heart muscle.

Clinically, it is well known that various cardiac disturbances take place during the early stages of syphilis, such as, tachycardia, bradycardia, arrhythmias and syncope. It is doubtful, however, whether these are due to a true specific myocarditis.

It is obvious that this question is very important. If there is a specific myocarditis in early syphilis, there is a foundation laid for the various forms of myocardial syphilis said by Warthin to occur in the later stages of the disease. (Active syphilitic myocarditis, chronic syphilitic myocarditis and fibroid myocarditis with acute exacerbation).

I am of the opinion that the heart muscle is not favorable soil for the growth of treponema pallidum. Because of the firm, ceaseless contractions, it is too active a place. The oxygen content is too high. I believe the strong muscle contractions favor lymphatic drainage towards the aortic arch and help in ridding the myocardium of the organisms.

Those remaining and surviving may rest for many years without doing appreciable damage. The finding, therefore,

of *a spirochete* in the heart muscle in late syphilis, perhaps surrounded by a few lymphocytes, may mean nothing more than an insignificant historical landmark. In a similar manner spirochetes may often rest in the skin of latent syphilitics, leaving no gross, and little microscopic evidence of their presence. Yet syphilis may be transmitted to rabbits by inoculation.

It is of interest to note that very few have ever been able to find spirochetes in the myocardium in acquired syphilis, although most careful and painstaking technic has been used. Furthermore, in using the Warthin-Starry technic, it has been repeatedly shown that artifacts indistinguishable from spirochetes may be obtained by staining cover slips alone, without any tissue.

Saphir[3] in a review of the recorded cases of syphilitic myocarditis in literature states: "A critical consideration reveals that morphologically the diagnosis of syphilitic myocarditis cannot be made in any of the reviewed cases without the presence of gummas." Furthermore, perivascular infiltrations of lymphocytes in the myocardium; lymphocytes, plasma cells and endothelial cells in the interstitial tissue; and polynuclears may be found in the myocardium in cases of coronary sclerosis especially in cases in which there has been infarction and in cases of rheumatism and other infections. They are not pathognomonic of syphilis.

### The Nervous System

In the stage of spirochetemia, innumerable spirochetes reach the brain by way of the carotid circulation.

Many of these eventually reach the pia-arachnoid, chiefly over the base of the brain. Reproduction is followed by the characteristic, cellular reaction.

Even as early as the stage of the chancre, an increase in the cell count of the spinal fluid may occur, denoting the existence already of an exudative process in the leptomeninges.

In the secondary stage, spirochetes have been found in the spinal fluid, both by inoculation and the microscope.

While infection of the nervous system is common and occurs early in the disease, the actual development of syphilitic disease is much less so, and only around 20 per cent of all syphilitics show during their disease meningovascular symptoms.

That all syphilitics do not develop neurosyphilis, tabes or paresis is due to many factors, such as dosage, resistance of host, immunity, and possibly differences in strains of organisms.

The common location for early neurosyphilis is over the base of the brain, where when the lesion is visible, a gelatinous exudate is seen over the interpeduncular spaces, or a milkiness so slight that it may easily be overlooked. This location accounts for the early involvement of the third, fourth and sixth cranial nerves with symptoms of diplopia, strabismus, etc.

The manner in which the spirochetes gain access to the subarachnoid spaces over the base of the brain is of great interest.

In tuberculous meningitis the tubercles are located, chiefly, in the Sylvian fissures along the course of the middle cerebral arteries. For years they were interpreted as hematogenous in distribution, springing from the vessels of the pia-arachnoid. While this appeared plausible, it has for many reasons, never satisfied critical pathologists.

Rich[4] then demonstrated, experimentally, that the meninges could not be infected by direct injections of tubercle bacilli into the carotid arteries, but typical tuberculous meningitis could be produced by subarachnoid injections. He regarded a primary infection of the choroid plexus, a hematogenous one of course, as the essential factor in the production of tuberculous meningitis, the bacilli entering the interventricular fluid and finally reaching the subarachnoid spaces over the base of the brain.

Lewkowicz[5] called attention to the same mode of infection in meningococcus meningitis.

I am of the opinion, that the same anatomical route occurs in syphilis, the spirochetes entering the lateral ventricles by way of the choroid plexuses. Because of the large size of the ventricles, their smooth walls and the downward flow of spinal fluid, the spirochetes are rapidly washed out of the ventricular system into the basal cisterna where they finally lodge in the quiet and restful interstices of the subarachnoid spaces over the base of the brain.

Such a conception best explains the location of early neurosyphilis and the logical development from it of meningoencephalitis and general paresis. In paresis, the granular ependyma of the lateral and fourth ventricles is pathognomonic, a heaping up of neuroglia proliferation probably due to spirochetal rests which have been caught in the ependyma.

Such a conception warrants careful histological study of the choroid plexuses in this disease, which seem to have been overlooked.

### Latent Stage

In the latent stage of syphilis, the organisms are held in check by the local and systemic defense, the innumerable, minute, imperfectly healing foci producing immunity.

Local foci may flare up at any time, discharging a shower of spirochetes into the circulation, or into a lymphatic drainage area. Reinfection takes place, followed usually, by reproduction, typical lymphocytic cellular reactions, with consequent fibrosis and suppression of the infection. In many of these foci all the spirochetes are not killed and relapses occur.

This flareup of partly extinguished foci with consequent imperfect healing and vascular changes, results in damage to the surrounding tissues and parenchyma and the most dangerous stage of syphilis, the degenerative phase begins.

The clinical picture of this latent stage is usually characterized by prolonged absence of symptoms. Relapses are

characterized by fewer, more localized and destructive lesions due to the pronounced vascular changes and possibly to allergy. Spirochetes are scant in number and the patient is clinically not infectious.

### Late Syphilis—Gummatous Stage

In late syphilis, due to the allergy or hypersensitiveness, and especially to the chronic vascular changes, gummas are prone to develop.

Gummata are gummy, tumor-like masses varying in size from those just visible to larger masses several inches in diameter. They are not to be confused with the miliary gumma. They may occur in any organ or tissue.

They contain very few spirochetes and the lesion is not clinically infective. They are circumscribed and composed of granulation tissue with a center of caseation due to ischemia produced by the obliterating endarteritis. There are collections of lymphocytes and plasma cells around the center of caseation, together with a few giant cells. On the edge, proliferating fibroblasts and a definite fibrous capsule may be noted. The result is extensive sloughing with destruction of parenchyma and enormous scarring.

On account of their size, gummata usually produce symptoms and are easily diagnosed. They are consequently becoming less frequent.

Gummas are more likely to be encountered in the brain, where on account of their size, they must be differentiated from other cerebral tumors; in the calvarium, where they cause extensive destruction of the skull, fortunately infrequently seen, nowadays; in the larynx, where they produce hoarseness and sometimes cause death from asphyxiation; in the mediastinum, where they represent the only common form of thoracic syphilis; in the lung, where they are infrequent; in the liver, where they lead to extensive destruction with the production of the well known hepar lobatum; in the heart muscle, where they are rare, being only seen in large autopsy services and usually occurring on the in-

terventricular septum; in the testes, where they have often been erroneously removed for malignancy; in the rectum, where they produce strictures; in the bones, commonly in the tibiae, where they must be diagnosed from other bone tumors; and in the skin, usually over the legs, where they may produce extensive ulceration and scarring.

### Late Syphilis—Degenerative Stage

Syphilis is frightful, not because of destructive lesions of the skin and bones, but because of the late, insidious complications.

From 10 to 15 to 20 years after the infection, when the patient has forgotten all about his disease, after years of apparent health, and at the age when he is carrying his heaviest responsibilities, he is suddenly confronted with the fact that he has been gradually developing a serious, irreparable, and eventually, fatal disease of his nervous and cardiovascular systems.

This degenerative stage is the result of the imperfect healing of the innumerable, metastatic, miliary gummata which occur throughout the disease, in any organ or tissue of the body.

The small, microscopic perivascular collection of lymphocytes and plasma cells forming the miliary gumma is the characteristic histological unit of syphilis, as is the tubercle in tuberculosis and the submiliary tubercle in rheumatic fever.

Due to imperfect healing and incomplete sterilization there is a constant flaring up of these foci throughout the disease. New adjacent and far distant foci are formed by reinfection. Reproduction, a cellular defense reaction, fibrosis and imperfect healing take place. In time this vicious cycle causes irreparable damage to the parenchyma and surrounding body tissue. Serious disease, especially of the nervous and cardiovascular systems, results.

In the nervous system, the early neurosyphilis, if not cured, may become markedly meningoencephalitic in type

and paresis develops. In this disease, the spirochetes become very numerous, unlike that in any other late lesion in syphilis. Or tabes may develop, usually due to this same gummatous infiltration of the posterior ganglia, the changes in the posterior columns being entirely those of secondary degeneration. Hence, spirochetes are very scant in the cord.

### Syphilis of Aorta and Heart

In syphilis of the aorta and heart the main lesion is usually in the first portion of the aortic arch.

During the stage of spirochetemia, we have already noted the countless metastatic foci established in the skin of the entire body (as manifested by the rash), in the mucous patches in the mouth and pharynx, and over the genitals. About each focus, reproduction takes place, characteristic cellular reactions and then subsidence and healing. On healing the remaining spirochetes drain into the regional lymph-nodes. From the face, mouth, throat, chest and upper extremities the final drainage must be into the mediastinal nodes.

Furthermore, this is augmented by the drainage into these same nodes of the spirochetes coming from the lungs.

The hilus and mediastinal nodes then become, in fact, the largest and most important group of nodes draining spirochetes from the parenchymatous organs and tissues and the largest collecting stations or reservoirs for the storage and destruction of spirochetes.

The lymphatic network leading to these glands and away from them is enormous. The moving of the parts during respiration, greatly increases the possibility of retrograde lymphatic permeation and embolism. Although some pathologists ridicule retrograde lymphatic drainage, it is a well established mode of metastasis in cancer.

The most important retrograde extension from these nodes would be to the first portion of the aorta.

The main and most important lesion in nearly all cases

of acquired syphilis of the aorta is a supravalvular sclerosis. Most of the other changes and phases of cardiac syphilis depend upon this lesion.

The earliest lesions are microscopic and occur around the vasa vasorum in the adventitia of the root of the aorta where there is seen a collection of lymphocytes and plasma cells, lying, probably, in the perivascular lymph-spaces. Stained sections may show spirochetes in these areas, but usually they are found with difficulty. Small, miliary gummata are formed in the adventitia.

There follows a secondary invasion of the media with consequent breaking up of elastica and weakening of the vessel wall. Obliterating endarteritis of the vasa vasorum is common. The lesion develops to a stage at which it can be recognized with the naked eye. The earliest patch is usually triangular and situated just above the commissures distal to the attachment of the aortic cusps. The base of the triangle is usually pointed upward. There is a gray or slightly yellowish elevation with steep edges, rubbery and smooth on top, but marked by shallow, parallel or stellate furrows.

The process spreads in a horizontal manner around the root of the aorta (girdle of Venus). Distally it often extends to the mouths of the great vessels springing from the aortic arch. The orifices of these arteries may often be narrowed to a marked degree. The sclerosis may diffusely involve the whole aortic arch and extend into the thoracic aorta.

Histological study shows that the gummatous process starting and most pronounced in the adventitia, has infiltrated the media, breaking up and pushing aside elastic fibers, and has gained access to the subintimal tissue of the aorta where there is less resistance to further infiltration.

I speak of the whole process as a sclerosis because the lesion found at autopsy is in the nature of a deforming

scarring defect, due to the insidious gummatous infiltration, with imperfect healing and fibrosis.

Acquired cardiac syphilis is, therefore, essentially a supravalvular sclerosis which may manifest itself in one or more of the following ways:

The first, most frequent and most dangerous is the production of an aortic regurgitation. In my series[6], aortic regurgitation occurred in about 60 per cent of syphilitic aortitis which result in death (combined hospital and medical examiners' cases), and in 36 per cent of cases of sudden death due to syphilis of heart and aorta.

The regurgitation was always a secondary extension from a syphilitic aortitis and usually occurred as the result of a descending process. Extension of the syphilitic gummatous process through the media into the subintimal spaces producing the triangular patches, continues in the direction of the attachment of the aortic cusps, usually following the lines of least resistance, which is alongside of and between the fan-shaped subintimal fibers, the remnants of those fibers forming originally the aortic cusps.

The result is a pushing apart of the cusps at their attachments by the gummatous and sclerosing process. Sometimes the attachments of the cusps may be separated by at least 1 cm. Often, just a furrow exists between the attachments of the adjacent cusps, which are thickened and infiltrated. This widening of the commissures is the earliest sign of aortic regurgitation, and is practically the main factor in its production.

The aortic valve may also be attacked by the gummatous process ascending through the sinus of Valsalva. In this process only the aortic layers of the cusps will be involved.

The syphilitic lesion does not as a rule reach the free edges of the valves. The characteristic thickening and rolling of the free edges of the cusps in syphilis is a functional adaptation to the primary dilatation of the aortic ring

and the thickening is a functional marginal sclerosis made worse by the mechanical effect of the regurgitant blood stream. The endocardial thickenings on the interventricular septum below the cusps is also mechanical due to regurgitant stream.

The aortic regurgitation is often combined with narrowing or atresia of the coronaries, and it is sometimes superimposed upon an old aortic aneurysm.

The heart nearly always shows marked hypertrophy and often dilatation, especially of the left ventricle.

The main myocardial lesion is hypertrophy, seen on gross and microscopic examination. Other lesions are infrequent and of no great significance.

The irreparable sclerotic lesion is not as a rule favorably influenced by specific treatment. Sudden death is due to acute dilatation or to an anginoid type of failure when the coronaries are involved. When death is delayed it is usually due to failure of the congestive type.

As a rule patients do not survive a two-year period after the diagnosis is made. Exceptional cases may live for many years.

The second main danger of syphilitic supravalvular sclerosis is stenosis and atresia of the coronary arteries. In my series this occurred in about 30 per cent of syphilitic aortitis resulting in death and in about 15 per cent of sudden death due to syphilis of aorta and heart.

The process is always a narrowing, often to complete atresia, of one or both arteries, due to encroachment upon their orifices in the aortic wall by the syphilitic process. Syphilis of the coronaries beyond the aortic wall is rare if we exclude a small amount of adventitial gummatous infiltration which spreads down from the aortic wall and is rarely seen over 1 cm. beyond the orifice of the artery.

If the coronary orifices are congenitally high placed above a base line drawn through the upper attachments

of the aortic cusps, they are much more liable to narrowing than if they arise normally in the sinuses of Valsalva.

The heart is usually normal in size, or occasionally slightly enlarged in the pure forms of this lesion. The muscle is quite normal in appearance and usually shows no evidence of any specific myocardial lesions. Occasionally an inanition atrophy similar to brown atrophy is seen.

Unlike coronary occlusion in arteriosclerosis, in syphilis the process is a very slow and gradual one. Compensatory circulation is often established and keeps the individual alive and often in apparent health for a long time, even with both coronaries completely occluded, when the thebesian circulation supplies the heart muscle.

Myocardial infarction, therefore, practically does not occur in these cases and its absence is almost pathognomonic.

Sudden death is difficult to explain on account of the long duration of the stenosis. Physical strain, fright, emotions, etc., seem to play an important rôle. Syphilitic angina usually occurs in this type of case and not in other forms of cardiac syphilis. It is usually anginoid with atypical symptoms, but sometimes resembles the angina of arteriosclerosis, and even an occlusion in rare instances.

Specific treatment in these cases is usually contraindicated, because of the danger of a Herxheimer reaction or too rapid healing causing a therapeutic paradox.

The third main danger of syphilitic supravalvular sclerosis is aortic aneurysm. In my series, this occurred in 10 per cent of cases of syphilitic aortitis resulting in death but was the most common cause of sudden death, being the direct cause of death in about 37 per cent of medical examiners' cases.

The aneurysm is due to weakening of the aortic wall by the syphilitic, gummatous infiltration. A high maintained diastolic pressure, when the aortic valve is not in-

volved and there is no regurgitation, is usually the important factor in the aneurysmal dilatation.

Cases of long duration are frequently associated with a regurgitation which has been superimposed after the aneurysm has existed for many years.

If there is no regurgitation and the aneurysm is not near enough to the aortic ring to produce dilatation, the heart is usually normal in size, or only moderately hypertrophied.

Death is usually sudden and due to rupture. If the coronaries are involved it may be sudden with, or without, anginoid symptoms. Slow death is due to failure of congestive type, or is a result of pressure on the surrounding structures.

Pain, the main symptom, can often be relieved by proper specific treatment, although the physical signs may increase. Specific treatment is less dangerous and gives better results than in regurgitation or coronary stenosis.

### Other Arterial Lesions

Of all the arteries, the aortic arch is the chief location for miliary gummatous lesions in late syphilis. The process in the aorta often reaches the great vessels of the aortic arch and produces a narrowing of their orifices.

Syphilis also is fairly frequently seen in the carotid arteries, and carotid aneurysms are by no means rare. This should be expected when we recall the lymphatic drainage from the neck and nasopharynx in syphilis, towards the mediastinum by way of the deep lymphatics. Typical lesions in the femoral arteries have been noted but they are of less frequent occurrence.

It is extremely rare to see a gangrene of the lower extremities which could be definitely laid to syphilitic arteritis. This is accounted for by the fact that the spirochetes from the skin rashes and lesions on the legs drain by way of the superficial lymphatics to the inguinal nodes and away from the peripheral arteries of the legs.

Syphilis is frequently seen in the cerebral arteries as a periarteritis, and because of the small caliber of the vessels, an added obliterating endarteritis is liable to produce thrombosis rather than aneurysm.

It may be stated, therefore, that aside from the aortic arch and the cerebral arteries, syphilis plays very little part in lesions of the other arteries.

### Other Interstitial and Degenerative Lesions

An interstitial form of pulmonary syphilis, although reported by many clinicians and roentgenologists, is an uncertain diagnosis at autopsy, and as Boyd[7] states, forms one of the most nebulous pathological entities.

Hepatic syphilis in the form of an interstitial cirrhosis is another doubtful pathological entity, the main lesion in the liver being one of multiple large gummas with extensive scarring (hepar lobatum).

An interstitial form of syphilitic orchitis occurs quite frequently, and is much more common than the gumma of the testes. It is often seen at autopsy as the only historical landmark of syphilis and demonstrates the necessity of the routine examination at autopsy of the testes. The testicle on cut section shows pale, grayish, hyaline streaks, sometimes none of the brownish parenchyma being visible, and the tubules string out with difficulty.

Occasionally a splenomegaly is seen in late syphilis, associated with a positive Wassermann and an anemia, the clinical picture being indistinguishable from Banti's disease. In these cases, there is no improvement after antiluetic treatment unless the spleen is removed surgically, the spirochetes seeming to be locked up in the diffuse fibrosis and resisting destruction by treatment. Some authorities have stated that the Banti's syndrome is always syphilitic, but this must be incorrect.

### Summary

The development of syphilitic destructive lesions in the nervous and circulatory systems has been given in a

sketchy way outlining certain theories which have appeared to be as near the correct interpretation as we can attain by our present knowledge.

From a clinical and pathological standpoint, I believe that we should regard syphilis of the aorta and heart as an acquired disease (congenital cases being rare) developing insidiously and showing symptoms years after the initial infection.

Death in acquired syphilis of the aorta and heart is almost always due to an aortic regurgitation, or to narrowing or atresia of the coronary arteries, or to the production of an aortic aneurysm, or to any combination of the three great dangers of syphilitic aortitis. Death is due occasionally to unusual lesions caused by syphilis, such as spontaneous rupture of the aorta, dissecting aneurysm, isolated gumma of the heart muscle, miliary aneurysms, etc.

Specific lesions of the myocardium and of the coronary arteries beyond the aortic wall are infrequent, they have been greatly exaggerated, and when they occur are so slight in extent as to be of little practical importance. They rarely embarrass cardiac action, are insignificant in the production of cardiac failure and the slower modes of cardiac death, and are of little importance in explaining sudden death.

The myocardium in syphilis is frequently normal. When the aortic valve is involved, the main myocardial lesion is hypertrophy. Inanition atrophy is occasionally encountered when there is a slow stenosis and atresia of both coronary orifices. Specific lesions of the myocardium are rare, and, when they occur, are slight in extent and of little practical importance.

It is safer and better to assume that the coronaries distal to the aortic wall are usually normal in pure, uncomplicated syphilis, and that coronary occlusions, anemic infarcts, necrosis of heart muscle, replacement fibrosis, aneurysms of ventricular walls, and fibrous myocarditis are almost entirely due to coronary injury dependent upon an

arteriosclerotic process and have nothing to do with syphilis. That rheumatism and other infections produce forms of interstitial myocarditis is obvious. But it appears that syphilis does not play an important rôle in the production of such lesions.

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## GENERAL DISCUSSION

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I am sure that we have all enjoyed the papers of this evening very much, and as for myself, I am certain that I have profited greatly by them. I have been particularly charmed by the splendid presentation which Dr. Martland has made concerning the pathology of vascular syphilis, a subject in which I have been very much interested for many years.

In this regard I wish especially to commend the beautiful slides and charts which Dr. Martland presented, tho I was much distressed to have him pass over without comment and rapidly, a slide which showed most beautifully the syphilitic changes produced in the myocardium, a subject which I regret Dr. Martland has failed to study with his usual care and fair mindedness. I am certain that the manes of Dr. Warthin would have been horribly shocked had they heard the cursory way with which Dr. Martland looked on this one phase of the subject, for he is so broad, so convincing and so thoro in all the other phases of the subject.

For many years it was my privilege to visit the luetic cases under the charge of the late Dr. Fordyce at the City Hospital, a service which adjoined my own service in Medicine, and I also during the early period of the War had under my frequent observation all the cases of primary and secondary lues which entered the Base Hospital at one of our large mobilization camps. Altho my practice now rarely comes in contact with cases of either primary or secondary lues, I feel that I am still justified in speaking with some assurance as regards the cardiovascular changes in this phase of syphilis also.

I have never seen a single instance in which cardiovascular symptoms or pathology became evident in, or were exaggerated by, primary syphilis. Cardiovascular changes in secondary lues are also exceedingly infrequent as compared to their occurrence in the late phases of the disease. None the less Carroll and I collected some 41 instances of such disease some years ago. Three of our cases terminated fatally very much after the manner of the cases in this stage which have been cited by Warthin, Wile and Stokes.

I am convinced that proper anti-syphilitic treatment of the primary and secondary stages of syphilis prevent the appearance of serious cardiac lesions due to syphilis in almost 100 per cent of instances. Because of what has been said this evening, however, I must point out the well accepted fact among clinicians that arsenic is a very dangerous drug to employ in cardiovascular syphilis except in instances which have previously been brought very well under the effects of those other still potent, tho old, specifics in this disease, namely mercury, the iodides and more recently bismuth.

Surely no one who has seen the remarkable lesions which Dr. Martland's slides exhibited tonight can expect any drug to perform miracles and save life when such extensive and vital damage has been committed as was shown in the slides of this evening. There can however remain little doubt in the minds of those clinical students who have conscientiously employed proper therapeutic measures in the secondary and early tertiary stages of cardiovascular syphilis, who can fail to feel that such cases properly treated probably represent the most definitely curable form of heart disease with which we are familiar.

Dr. Martland has most brilliantly demonstrated the character and gravity with which late syphilis affects the aorta. If as he apparently feels, muscular syphilis in so far as the heart is concerned, is unusual, it is very difficult to explain the clinical results which competent clinicians obtain in the management of most relatively early clinical

evidences of cardiac syphilis and even in many of the late stages which one meets in practice.

Death from aortic disease is a difficult phenomenon to explain on a logical basis from purely aortic lesions in syphilis if we must assume that the myocardium possesses the strange and unique immunity against the infection which would then represent in so far as I know, about the only tissue in the body of mesodermal origin which is not involved in this protean infection. To me as a clinician and as a some time pathologist, the symptoms manifested in most cases of cardiovascular syphilis are those of myocardial involvement in association, it is true, usually with more or less aortic disease.

I again wish to express my indebtedness to the speakers of the evening, and particularly to Dr. Martland, my friend and opponent, and also especially to the very clear and helpful discussion of the new treatment of cerebrospinal syphilis, which has been so splendidly presented tonight by our colleague from Harvard University.

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Cohen, P. The British system of social insurance.
[London], Allan, 1932, 278 p.

Doane, L. L. Guide to localized bi-terminal tonsillar coagulation.
Butler, Pa., Washburn, [1931], 112 p.

Ergebnisse der Enzymforschung. Hrsg. von F. F. Nord und R. Weidenhagen.
Leipzig, Akademische Verlagsgesellschaft, 1932, v. 1.

Fairweather, S. D. Flatfoot: the true nature, cause and rational cure.
London, Bale, 1932, 76 p.

Forbes, J. G. Diphtheria, past and present.
London, Bale, 1932, 832 p.

Goodall, J. R. Puerperal infection.
Montreal, 1932, 189 p.

Haggard, H. W. The lame, the halt, and the blind.
N. Y., Harper, 1932, 420 p.

Harris, H. California's medical story.
San Francisco, Stacey, 1932, 421 p.

Kelly, H. A. and Ward, G. E. Electrosurgery.
Phil., Saunders, 1932, 305 p.

Lebermann, F. Der Wasserversuch als Nierenfunktionsprüfung.
Dresden, Steinkopff, 1932, 145 p.

Leroy, O. Le chevalier Thomas Browne.
Paris, Gamber, 1931, 422 p.

Loeper, M.; Tanon, L.; Turpin, R. [et al.]. Poumons et tuberculose.
Paris, Masson, 1932, 378 p.

Maternity Center Association, N. Y. Maternity handbook.
N. Y., Putnam, 1932, 178 p.

Monod, R. C. Tactique opératoire des annexes de l'utérus.
Paris, Doin, 1931, 162 p.

Needham, D. M. The biochemistry of muscle.
London, Methuen, [1932], 166 p.

New York Academy of Dentistry. The New York academy of dentistry; an historical sketch of the first decade, 1921-1931, by B. P. Palmer.
[N. Y.], N. Y. Academy of Dentistry, 1932, 81 p.

Peritz, G. Die Nervenkrankheiten des Kindesalters. 2. Aufl.
Leipzig, Fischer, 1932, 688 p.

Piney, A. and Wyard, S. Clinical atlas of blood diseases. 2. ed.
London, Churchill, 1932, 105 p.

Polu, R. La cholestérolémie des tuberculeux pulmonaires.
Paris, Maloine, 1931, 174 p.

Practitioner's (The) library of medicine and surgery.
N. Y., Appleton, [1932], v. 1-2.

Priesel, R. and Wagner, R. Die Zuckerkrankheit und ihre Behandlung im Kindesalter.
Leipzig, Thieme, 1932, 211 p.

Schultz, J. H. Das autogene Training.
Leipzig, Thieme, 1932, 305 p.

Smith, R. W. I. English-speaking students of medicine at the University of Leyden.
Edinburgh, Oliver, 1932, 258 p.

Special cytology. Edited by E. V. Cowdry. 2. ed.
N. Y., Hoeber, 1932, 3 v.

Spillmann, L.; Verain, M. and Weis, J. Le pH en dermatologie.
Paris, Masson, 1932, 194 p.

Stephens, G. A. The heart and spleen in health and disease.
London, Lewis, 1932, 139 p.

Thomson, (Sir) J. A. Scientific riddles.
London, Williams, 1932, 384 p.

Tjaden, H. C. Bremen und die bremische Aerzteschaft seit dem Beginne des 19. Jahrhunderts.
Bremen, v. Halem, [1932], 239 p.

Welch, A. S. Clinical interpretation of laboratory reports.
Phil., Blakiston, [1932], 366 p.

Winkler, A. Die Perkussion der Lungenspitzen.
Wien, Haim, 1932, 135 p.

## A Selected List of New Periodicals Added in 1932

### (January to June)

Archiv für Entwicklungsgeschichte der Bakterien.
Berlin, vol. 1, 1931.

Cleveland Clinic quarterly.
Cleveland, O., vol. 1, 1932.

Ergebnisse der Enzymforschung.
Leipzig, vol. 1, 1932.

Journal of cellular and comparative physiology.
Philadelphia, vol. 1, 1932.

Journal of the Medical Association of the State of Alabama.
vol. 1, 1931.

Maandschrift voor kindergeneeskunde.
Leiden, vol. 1, 1931.

Medical annals of the District of Columbia.
Washington, vol. 1, 1932.

Modern concepts of cardiovascular disease.
N. Y., vol. 1, 1932.

National Tuberculosis Association. Social research series.
N. Y., no. 1, 1932.

Nutrition. Annales cliniques, biologiques, thérapeutiques.
Paris, vol. 1, 1931.

Nutrition abstracts and reviews.
Aberdeen, vol. 1, 1931.

Psychoanalytic quarterly.
N. Y., vol. 1, 1932.

Revue de la presse médicale polonaise.
Warsaw, vol. 1, 1932.

Zeitschrift für Vitaminforschung.
Berlin; Bern, vol. 1, 1932.

## DEATHS OF FELLOWS OF THE ACADEMY

CHARLES AUGUSTUS LEALE, M.D., 1261 Madison Avenue, New York City; graduated in medicine from Bellevue Hospital Medical College, New York City, in 1865; elected a Fellow of the Academy December 2, 1869; died, June 13, 1932. Dr. Leale was a Fellow of the American Medical Association, a member of the American Society for the Advancement of Science, a member of the County and State Medical Societies, a member of the Neurological Society and Consulting Physician to Bellevue and Allied Hospitals. He was the oldest Fellow of the Academy.

MICHAEL OSNATO, M.D., 121 East 60 Street, New York City; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1906; elected a Fellow of the Academy January 3, 1918; died, June 15, 1932. Dr. Osnato was a Fellow of the American Medical Association, a member of the County and State Medical Societies, a member of the American Psychiatric Society, the American Neurological Society, the Neurological Society, New York Society for Clinical Psychiatry, Director of the Neurological Department to Post-Graduate Hospital, Consulting Neurologist and Psychiatrist to the Central Islip and Manhattan State Hospitals, and Neurologist to Reconstruction Unit, Post-Graduate and Columbus Hospitals.

# OFFICERS OF SECTIONS AND AFFILIATED SOCIETIES, 1932-33

*Dermatology and Syphilology*, 1st Tuesday

| *Chairman* | *Secretary* |
|---|---|
| A. Benson Cannon | Louis Chargin |
| 371 Park Avenue | 1 West 85 Street |

*Surgery*, 1st Friday

| | |
|---|---|
| William Barclay Parsons, Jr. | Ralph Colp |
| 180 Ft. Washington Avenue | 111 East 88 Street |
| | (appointed pro tem) |

*Neurology and Psychiatry*, 2nd Tuesday

| | |
|---|---|
| Byron Stookey | Clarence P. Oberndorf |
| 151 East 83 Street | 112 West 59 Street |

*Historical and Cultural Medicine*

2nd Wednesday of November, January, March and May

| | |
|---|---|
| C. N. B. Camac | Howard Reid Craig |
| 76 East 56 Street | 175 East 79 Street |

*Pediatrics*, 2nd Thursday

| | |
|---|---|
| John Caffey | Harry Bakwin |
| Bard Hall, Haven Avenue | 132 East 71 Street |

*Ophthalmology*, 3rd Monday

| | |
|---|---|
| Mark J. Schoenberg | Algernon B. Reese |
| 1160 Park Avenue | 73 East 71 Street |

*Medicine*, 3rd Tuesday

| | |
|---|---|
| Robert F. Loeb | Henry J. Spencer |
| Presbyterian Hospital | 24 West 10 Street |

*Genito-Urinary Surgery*, 3rd Wednesday

| | |
|---|---|
| George F. Hoch | C. Travers Stepita |
| 115 East 61 Street | 2 East 54 Street |

*Otolaryngology*, 3rd Wednesday

| | |
|---|---|
| Charles J. Imperatori | David H. Jones |
| 108 East 38 Street | 140 East 54 Street |

*Orthopedic Surgery*, 3rd Friday

| | |
|---|---|
| Mather Cleveland | Paul C. Colonna |
| 115 East 61 Street | 59 East 54 Street |

*Obstetrics and Gynecology*, 4th Tuesday

| | |
|---|---|
| Francis W. Sovak | Frederick C. Freed |
| 117 East 72 Street | 59 East 54 Street |

*The New York Roentgen Society*, 3rd Monday

| *President* | *Secretary* |
|---|---|
| J. Bennett Edwards | C. Wadsworth Schwartz |
| 144 Woodridge Pl., Leonia, N. J. | 33 East 68 Street |

*Society for Experimental Biology and Medicine*, 3rd Wednesday

| | |
|---|---|
| Dayton J. Edwards | A. J. Goldforb |
| First Avenue and 28 Street | Convent Avenue and 139 Street |

*Harvey Society*, 3rd Thursday

| | |
|---|---|
| Alfred F. Hess | Edgar Stillman |
| 16 West 86 Street | 22 East 69 Street |

*New York Pathological Society*, 4th Thursday

| | |
|---|---|
| Paul Klemperer | Maurice N. Richter |
| 378 Central Park West | 630 West 168 Street |